

Scientific and Technical Information Center

SEARCH REQUEST FORM

Date: 10/11/01 Requester's Full Name: DAVID LUKTON Examiner #: 71263
Art Unit: 1653 Phone (306) 3213 Serial Number: 09/355210
Results Format Preferred (circle): PAPER DISK E-MAIL

Title: Monocyclic Compounds with four Bifunctional residues having NK-2 antagonist action

Applicants: GIORGI, RAFFAELLO; PIRARI, ROSARIO;
GIORGI, ALBERTA; GIORGI, CHIARA; PIRARI, ROSARIA;
GIORGI, GABRIELE; PIRARI, ROSARIA; DI BUGNO, CRISTINA; GIANNOTTI,
DANILO; MAGGI, CARLO ALBERTO;

Earliest Priority Date: 2/7/97

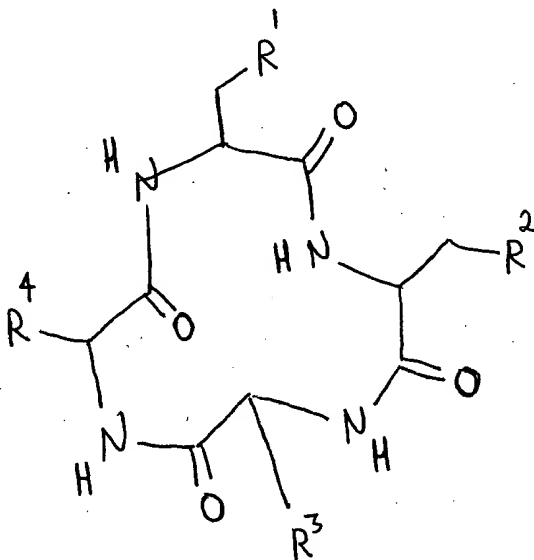
Applicants are claiming the compounds below

R1 = phenyl, imidazole, or indole

R2 = phenyl, imidazole, or indole

R3 = hydrogen or alkyl or benzyl; or R3 is the side chain of tryptophan or histidine

R4 = anything



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OCT 11 2001
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STAFF USE ONLY

Point of Contact:
Searcher: Alex Waclawiw
Technical Info. Specialist
CM1 12C14 Tel: 308-4491
Searcher Location: _____
Date Searcher Picked Up: 10-15-01
Date Completed: 10-15-01
Searcher Prep & Review Time: 15
Online Time: 28

Type of Search
____ NA Sequence (#)
____ AA Sequence (#)
2 Structure (#)
____ Bibliographic
____ Litigation
____ Fulltext
____ Other

Vendors and Cost
☒ STN _____ Dialog
____ Questel/Orbit _____ Dr. Link
____ Lexis/Nexis _____ Westlaw
____ WWW/Internet
____ In-house sequence systems (list)
____ Other (specify)

Lukton 09/355,210

=> fil reg

FILE 'REGISTRY' ENTERED AT 10:03:15 ON 15 OCT 2001
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STRUCTURE FILE UPDATES: 14 OCT 2001 HIGHEST RN 362009-74-3
DICTIONARY FILE UPDATES: 14 OCT 2001 HIGHEST RN 362009-74-3

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER see
HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES
for more information. See STNote 27, Searching Properties in the CAS
Registry File, for complete details:
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=> d his 11-17

(FILE 'HCAPLUS' ENTERED AT 09:58:10 ON 15 OCT 2001)
DEL HIS Y

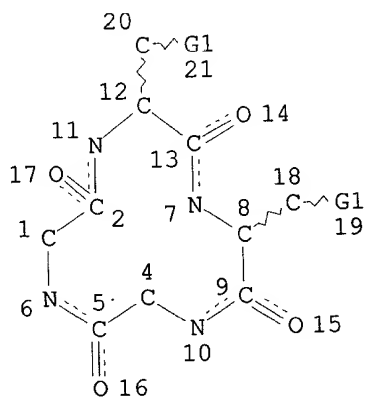
FILE 'REGISTRY' ENTERED AT 09:59:07 ON 15 OCT 2001
ACT LUKTON2/A

L1 STR
L2 STR
L3 (155)SEA FILE=REGISTRY SSS FUL L2
L4 11 SEA FILE=REGISTRY SUB=L3 SSS FUL L1

L5 1 S L4 AND CAOLD/LC
L6 1 S L4 AND USPATFULL/LC
L7 0 S L6 NOT (CA OR CAPLUS)/LC

=> d que stat 14

L1 STR



Cb @22 Hy @23 Hy @24

VAR G1=22/23/24

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

MLEVEL IS CLASS AT 12 13

GGCAT IS MCY UNS AT 22

GGCAT IS MCY UNS AT 23
 GGCAT IS PCY UNS AT 24
 DEFAULT ECLEVEL IS LIMITED
 ECOUNT IS UNLIMITED AT 12 13
 ECOUNT IS E6 C AT 22
 ECOUNT IS E3 C E1 N AT 23
 ECOUNT IS E8 C E1 N AT 24

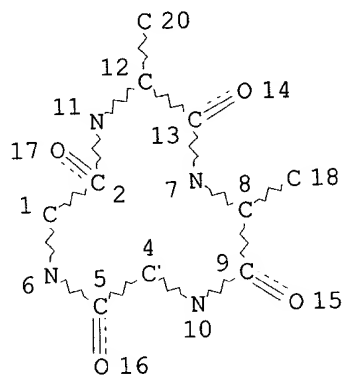
GRAPH ATTRIBUTES:

RSPEC I

NUMBER OF NODES IS 23

STEREO ATTRIBUTES: NONE

L2 STR



NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

MLEVEL IS CLASS AT 12 13

DEFAULT ECLEVEL IS LIMITED

ECOUNT IS UNLIMITED AT 12 13

GRAPH ATTRIBUTES:

RSPEC I

NUMBER OF NODES IS 18

STEREO ATTRIBUTES: NONE

L3 (155)SEA FILE=REGISTRY SSS FUL L2

L4 11 SEA FILE=REGISTRY SUB=L3 SSS FUL L1

100.0% PROCESSED 155 ITERATIONS

SEARCH TIME: 00.00.01

11 ANSWERS

=> d 15 ide can

L5 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS

RN 24181-12-2 REGISTRY

CN Cyclo(D-phenylalanyl-L-phenylalanyl-D-valyl-L-valyl) (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 1,4,7,10-Tetraazacyclododecane, cyclic peptide deriv.

CN Cyclo(D-phenylalanyl-L-phenylalanyl-D-valyl-L-valyl)

OTHER NAMES:

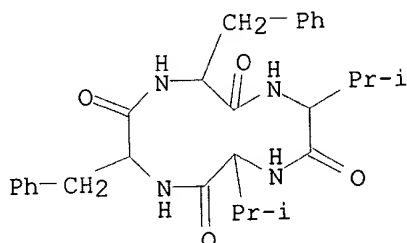
CN Cyclo(L-phenylalanyl-D-valyl-L-valyl-D-phenylalanyl)

CN Fugisporin

CN Fungisporin

FS PROTEIN SEQUENCE

DR 1412-12-0
 MF C28 H36 N4 O4
 LC STN Files: BEILSTEIN*, BIOSIS, CA, CAOLD, CAPLUS, CSCHM, NAPRALERT,
 TOXLIT
 (*File contains numerically searchable property data)



4 REFERENCES IN FILE CA (1967 TO DATE)
 1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
 4 REFERENCES IN FILE CAPLUS (1967 TO DATE)
 2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 133:340213
 REFERENCE 2: 93:6071
 REFERENCE 3: 88:23373
 REFERENCE 4: 71:124896

=> fil hcaplus
 FILE 'HCAPLUS' ENTERED AT 10:04:01 ON 15 OCT 2001
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FILE COVERS 1947 - 15 Oct 2001 VOL 135 ISS 17
 FILE LAST UPDATED: 14 Oct 2001 (20011014/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

This file supports REGISTRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

HCAplus now provides online access to patents and literature covered in CA from 1947 to the present. On April 22, 2001, bibliographic information and abstracts were added for over 2.2 million references published in CA from 1947 to 1966.

'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE

=> d his 18

(FILE 'HCAPLUS' ENTERED AT 09:59:39 ON 15 OCT 2001)

L8 12 S L4

=> d .ca hitstr l8 1-12

L8 ANSWER 1 OF 12 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2001:10082 HCAPLUS

DOCUMENT NUMBER: 134:80834

TITLE: Cyclic peptides and methods for modulating cell adhesion

INVENTOR(S): Blaschuk, Orest W.; Gour, Barbara J.

PATENT ASSIGNEE(S): McGill University, Can.

SOURCE: U.S., 80 pp., Cont.-in-part of U.S. 6,031,072.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

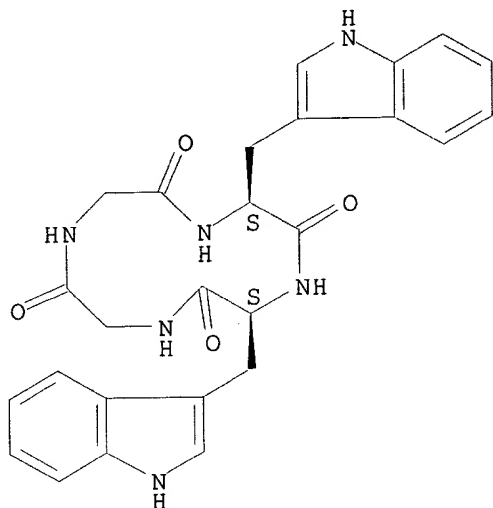
FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|-------------|-----------------|--------------------------------|
| US 6169071 | B1 | 20010102 | US 1997-996679 | 19971223 |
| US 6031072 | A | 20000229 | US 1997-893534 | 19970711 |
| US 6207639 | B1 | 20010327 | US 1998-115395 | 19980714 |
| WO 9933875 | A1 | 19990708 | WO 1998-CA1207 | 19981223 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BE, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 9918664 | A1 | 19990719 | AU 1999-18664 | 19981223 |
| PRIORITY APPLN. INFO.: | | | | |
| | | | US 1996-21612 | P 19960712 |
| | | | US 1997-893534 | A2 19970711 |
| | | | US 1997-996679 | A2 19971223 |
| | | | WO 1998-CA1207 | W 19981223 |
| AB | Cyclic peptides and compns. comprising them are provided. The cyclic peptides comprise a cadherin cell adhesion recognition sequence HAV. Methods for using the peptides and compns. for modulating cadherin-mediated cell adhesion in a variety of contexts are also provided. | | | |
| IC | ICM A61K038-00 ICS A61K038-12 | | | |
| NCL | 514004000 | | | |
| CC | 1-12 (Pharmacology) | | | |
| IT | Section cross-reference(s): 63 | | | |
| | 4248-64-0 | 27686-49-3 | 110590-64-2 | 113326-33-3 143304-79-4 |
| | 170032-25-4 | 202528-03-8 | 202528-15-2 | 222169-83-7 222169-86-0 |
| | 229971-60-2 | 229971-61-3 | 229971-64-6 | 229971-65-7 229971-67-9 |
| | 229971-68-0 | 229971-70-4 | 229971-72-6 | 229971-78-2 231282-25-0 |
| | 250268-78-1 | 313052-61-8 | 317320-03-9 | 317320-04-0 317320-05-1 |
| | 317320-06-2 | 317320-07-3 | 317320-08-4 | 317320-09-5 317320-10-8 |
| | 317320-11-9 | 317320-12-0 | 317320-13-1 | 317320-14-2 317320-15-3 |
| | 317320-16-4 | 317320-17-5 | 317320-18-6 | 317320-19-7 317320-20-0 |
| | 317320-21-1 | 317320-22-2 | 317320-23-3 | 317320-24-4 317320-25-5 |
| RL: | PRP (Properties) | | | |
| | (unclaimed sequence; cyclic peptides and methods for modulating cell adhesion) | | | |
| IT | 317320-20-0 | | | |
| RL: | PRP (Properties) | | | |
| | (unclaimed sequence; cyclic peptides and methods for modulating cell | | | |

adhesion)
 RN 317320-20-0 HCAPLUS
 CN Cyclo(glycylglycyl-L-tryptophyl-L-tryptophyl) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT:
 REFERENCE(S):

- 33
 (1) Alexander; Journal of Cellular Physiology 1993, V156, P610 HCAPLUS
 (2) Ali; J Med Chem 1994, V37(6), P769 HCAPLUS
 (3) Anon; EP 406428 B1 1991 HCAPLUS
 (4) Anon; WO 9104745 1991 HCAPLUS
 (5) Anon; WO 9208731 1992 HCAPLUS
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 12 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2000:894569 HCAPLUS

DOCUMENT NUMBER: 134:237780

TITLE: An evaluation of a novel safety catch linker for development of cyclic peptide libraries

AUTHOR(S): Bourne, G. T.; McGeary, R. P.; Golding, S. W.; Meutermans, W. D. F.; Alewood, P. F.; Smythe, M. L.

CORPORATE SOURCE: Centre for Drug Design and Development, University of Queensland, Brisbane, 4072, Australia

SOURCE: Pept. New Millennium, Proc. Am. Pept. Symp., 16th (2000), Meeting Date 1999, 98-99. Editor(s): Fields, Gregg B.; Tam, James P.; Barany, George. Kluwer Academic Publishers: Dordrecht, Neth.

CODEN: 69ATHX

DOCUMENT TYPE:

Conference

LANGUAGE:

English

AB A symposium on the authors' work using the 'safety-catch' linker approach to synthesis of cyclic peptides.

CC 34-3 (Amino Acids, Peptides, and Proteins)

IT 329966-10-1P 329966-12-3P 329966-14-5P

RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. of cyclic peptides using safety-catch linker)

IT 329966-10-1P 329966-12-3P

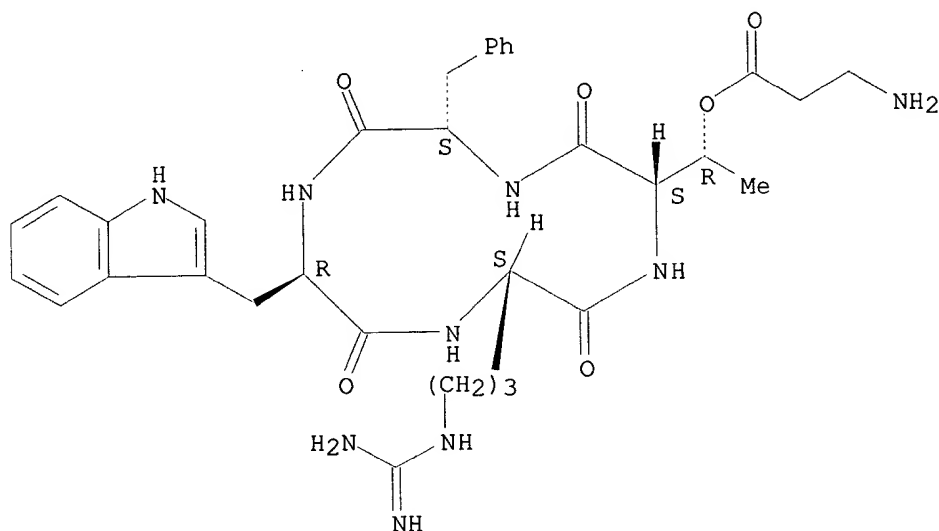
RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. of cyclic peptides using safety-catch linker)

RN 329966-10-1 HCAPLUS

CN Cyclo(L-arginyl-O-.beta.-alanyl-L-threonyl-L-phenylalanyl-D-tryptophyl)

(9CI) (CA INDEX NAME)

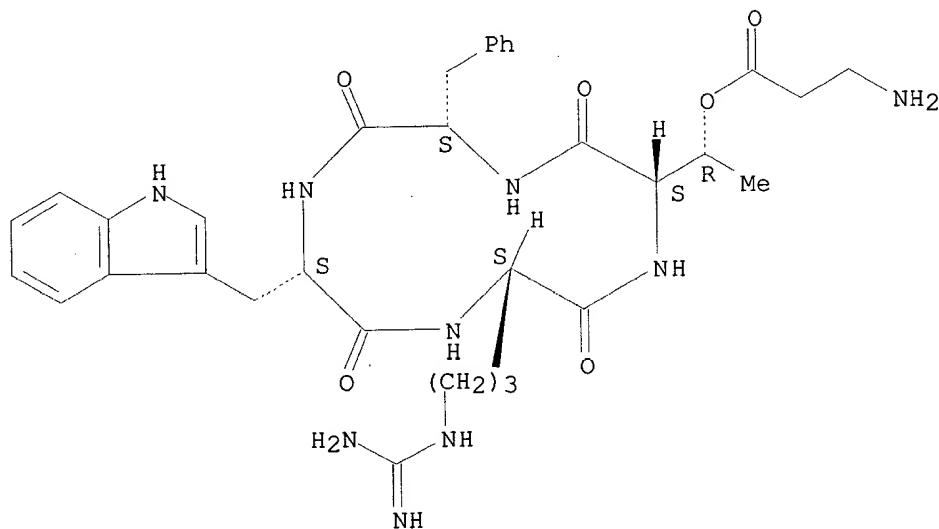
Absolute stereochemistry.



RN 329966-12-3 HCAPLUS

CN Cyclo(L-arginyl-O-.beta.-alanine-L-threonine-L-phenylalanine-L-tryptophan)
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

REFERENCE COUNT:
REFERENCE(S):

4

- (1) Bourne, G; J Org Chem 1999, V64, P3095 HCAPLUS
- (2) Flanigan, E; PhD Dissertation, Washington University 1971
- (3) Holmes, C; J Org Chem 1997, V62, P2370 HCAPLUS
- (4) Jensen, K; J Am Chem Soc 1998, V120, P5441 HCAPLUS

L8 ANSWER 3 OF 12 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2000:772490 HCAPLUS

DOCUMENT NUMBER: 133:340213

TITLE: Antibody conjugates for delivery of antimicrobial

INVENTOR(S): toxins
 Carlyle, Wenda C.
 PATENT ASSIGNEE(S): St. Jude Medical, Inc., USA
 SOURCE: PCT Int. Appl., 63 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| WO 2000064487 | A2 | 20001102 | WO 2000-US8389 | 20000330 |

W: BR, JP, ZA

RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
PT, SE

PRIORITY APPLN. INFO.: US 1999-298638 A 19990423

AB An antimicrobial conjugate (100, 120, 154) can be formed that includes an antibody (100, 122) or ligand bonded to an antimicrobial agent (106, 124). The antibody (102, 122, 154) or ligand has an affinity for microbial antigens or receptors. The antimicrobial conjugate (100, 120, 154) can be used alone or assocd. with biocompatible material (152) incorporated into a medical device (150). An antimicrobial conjugate (100, 120, 154) can be placed in contact with a soln. to eliminate viable microorganisms from the soln. In particular, the antimicrobial conjugate (100, 120, 154) can be used to reduce the risk of infection assocd. with the contact of a medical device with patient's bodily fluids or tissues.

IC ICM A61K047-48

CC 63-5 (Pharmaceuticals)

Section cross-reference(s): 1, 15

IT 56-75-7D, Chloramphenicol, antibody conjugates 57-92-1D, Streptomycin, antibody conjugates 60-54-8D, Tetracycline, antibody conjugates 61-33-6D, antibody conjugates 113-73-5D, Gramicidin S, antibody conjugates 114-07-8D, Erythromycin, antibody conjugates 1402-38-6D, Actinomycin, antibody conjugates 1404-90-6D, Vancomycin, antibody conjugates 1405-87-4D, Bacitracin, antibody conjugates 1406-11-7D, Polymyxin, antibody conjugates 2001-95-8D, Valinomycin, antibody conjugates 8011-61-8D, Tyrocidine, antibody conjugates 9008-54-2D, Circulin, antibody conjugates 11140-67-3D, Syringomycin, antibody conjugates 18524-67-9D, Mycobacillin, antibody conjugates 23155-02-4D, Phosphonomycin, antibody conjugates 24181-12-2D, Fungisporin, antibody conjugates 53571-13-4D, Malformin, antibody conjugates 67995-63-5D, Pardaxin, antibody conjugates 73590-58-6D, Omeprazole, antibody conjugates 103577-45-3D, Lansoprazole, antibody conjugates
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process);
 USES (Uses)

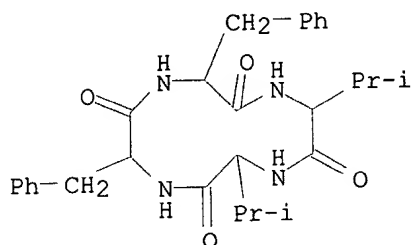
(antibody conjugates for delivery of antimicrobial toxins)

IT 24181-12-2D, Fungisporin, antibody conjugates
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process);
 USES (Uses)

(antibody conjugates for delivery of antimicrobial toxins)

RN 24181-12-2 HCAPLUS

CN Cyclo(D-phenylalanyl-L-phenylalanyl-D-valyl-L-valyl) (9CI) (CA INDEX
 NAME)



L8 ANSWER 4 OF 12 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2000:288753 HCAPLUS

DOCUMENT NUMBER: 133:164306

TITLE: Cyclic tetrapeptide hydroxamic acids related to

AUTHOR(S): trapoxin B inhibit histone deacetylase
Nishino, Norikazu; Tomizaki, Kin-Ya; Mimoto, Tsutomu;

CORPORATE SOURCE: Institute for Fundamental Research of Organic
Chemistry, Kyushu University, Fukuoka, 812-8581, Japan

SOURCE: Pept. 1998, Proc. Eur. Pept. Symp., 25th (1999),
Meeting Date 1998, 832-833. Editor(s): Bajusz,
Sandor; Hudecz, Ferenc. Akademiai Kiado: Budapest,
Hung.

DOCUMENT TYPE: CODEN: 68WKAY

LANGUAGE: English

AB A symposium report. Trapoxin B analogs, cyclic tetrapeptides contg.
.alpha.-aminosuberyl, .alpha.-aminoazelayl, and .alpha.-aminopimelyl
.omega.-hydroxamic acids, were prepd. and tested for inhibition of histone
deacetylase.

CC 34-3 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 7

IT 133155-90-5DP, Trapoxin B, analogs 221186-39-6P 221186-42-1P

221186-43-2P 221186-56-7P 221186-58-9P **221186-59-0P**

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic
preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of trapoxin B-related cyclic tetrapeptide hydroxamic acids as
histone deacetylase inhibitors)

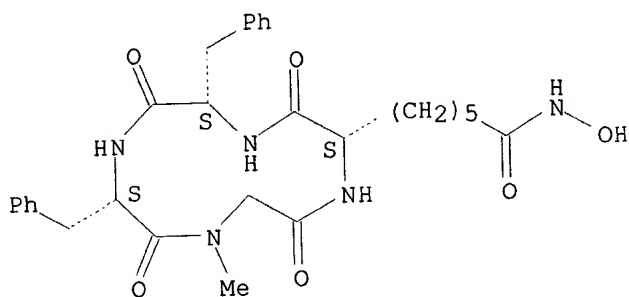
IT **221186-59-0P**

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic
preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of trapoxin B-related cyclic tetrapeptide hydroxamic acids as
histone deacetylase inhibitors)

RN 221186-59-0 HCAPLUS

CN Cyclo[N-methylglycyl-(2S)-2-amino-8-(hydroxyamino)-8-oxooctanoyl-L-
phenylalanyl-L-phenylalanyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT:
REFERENCE(S):

- 6
(1) Itazaki, H; J Antibiotics 1990, V43, P1524 HCAPLUS
(2) Kijima, M; J Biol Chem 1993, V268, P22429 HCAPLUS
(3) Nishino, N; Biochemistry 1978, V17, P2846 HCAPLUS
(4) Nishino, N; Chem Pharm Bull 1996, V44, P212 HCAPLUS
(6) Yoshida, M; J Biol Chem 1990, V265, P17174 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 12 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER:

1999:353256 HCAPLUS

DOCUMENT NUMBER:

131:130252

TITLE:

Histone deacetylase inhibitors based on trapoxin B

AUTHOR(S):

Tomizaki, Kin-Ya; Kato, Tamaki; Nishino, Norikazu;

CORPORATE SOURCE:

Yoshida, Minoru; Komatsu, Yasuhiko
Department of Applied Chemistry, Faculty of
Engineering, Kyushu Institute of Technology,
Kitakyushu, 804-8550, Japan

SOURCE:

Pept. Sci. (1999), Volume Date 1998, 35th, 181-184
CODEN: PSCIFQ; ISSN: 1344-7661

PUBLISHER:

Protein Research Foundation

DOCUMENT TYPE:

Journal

LANGUAGE:

English

AB A symposium report. Trapoxin B is a cyclic tetrapeptide contg. a unique amino acid, (2S,9S)-2-amino-8-oxo-9,10-epoxydecanoic acid (L-Aoe), whose epoxyketone moiety is supposed to react with mammalian histone deacetylase. The authors synthesized a trapoxin B analog, in which L-Aoe is replaced with L-aminosuberic hydroxamic acid [Asu(NHOH)]. The analog strongly inhibited a histone deacetylase from mouse B16/BL6 cells. Furthermore, the positions of D-amino acids in the trapoxin B hydroxamic acid analog were changed. In addn. to L-L-L-D-form [contg. L-Asu(NHOH)], L-L-D-L-, L-D-L-L-, and L-D-L-D-isomers were synthesized. The L-D-L-L- and L-D-L-D-isomers exhibited high inhibitory activity, while L-L-D-L-isomer was inactive.

CC 34-3 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 7

IT 58880-19-6, Trichostatin A 133155-90-5D, Trapoxin B, analogs contg.

aminosuberic hydroxamic acid deriv. 221186-39-6 221186-42-1
221186-43-2 221186-56-7 221186-57-8 221186-58-9 **221186-59-0**

221186-62-5 **234429-76-6** 234429-77-7

RL: BAC (Biological activity or effector, except adverse); BIOL
(Biological study)

(prepn. of hydroxamic analogs of trapoxin B as inhibitors of histone deacetylase)

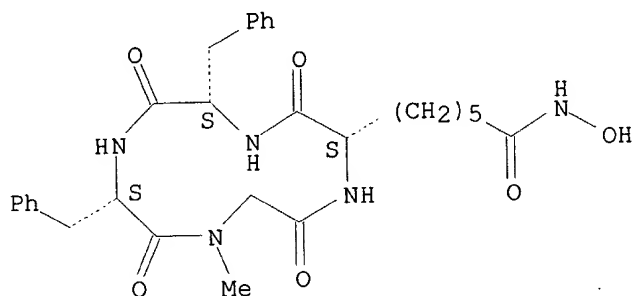
IT **221186-59-0 234429-76-6**

RL: BAC (Biological activity or effector, except adverse); BIOL
(Biological study)

(prepn. of hydroxamic analogs of trapoxin B as inhibitors of histone deacetylase)

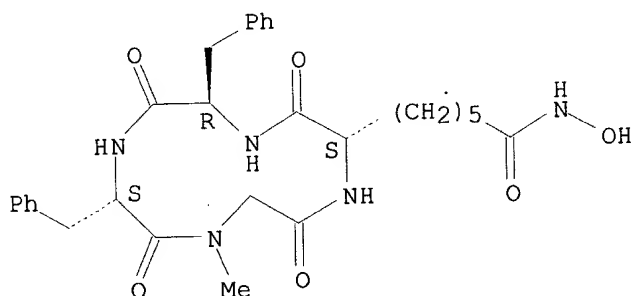
RN 221186-59-0 HCAPLUS
 CN Cyclo[N-methylglycyl-(2S)-2-amino-8-(hydroxyamino)-8-oxooctanoyl-L-phenylalanyl-L-phenylalanyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 234429-76-6 HCAPLUS
 CN Cyclo[N-methylglycyl-(2S)-2-amino-8-(hydroxymethyl)-8-oxooctanoyl-D-phenylalanyl-L-phenylalanyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT:
 REFERENCE(S):

- 14
 (1) Itazaki, H; J Antibiotics 1990, V43, P1524 HCAPLUS
 (2) Jacquier, R; Tetrahedron Lett 1984, V25, P5525 HCAPLUS
 (3) Kawai, M; Biochem Biophys Res Commun 1983, V111, P398 HCAPLUS
 (4) Kijima, M; J Biol Chem 1993, V268, P22429 HCAPLUS
 (5) Nishino, N; Chem Pharm Bull 1996, V44, P212 HCAPLUS
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 12 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1999:184270 HCAPLUS

DOCUMENT NUMBER: 130:237885

TITLE: Preparation of novel cyclic tetrapeptide derivatives as histone deacetylase inhibitors and MHC class-I molecule expression promoters

INVENTOR(S): Nishino, Norikazu; Yoshida, Minoru; Horinouchi, Sueharu; Komatsu, Yasuhiko; Mimoto, Tsutomu

PATENT ASSIGNEE(S): Japan Energy Corporation, Japan

SOURCE: PCT Int. Appl., 97 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|------------|
| WO 9911659 | A1 | 19990311 | WO 1998-JP3893 | 19980901 |
| W: AU, CA, JP, KR, NO, NZ, US | | | | |
| RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| AU 9888885 | A1 | 19990322 | AU 1998-88885 | 19980901 |
| AU 732299 | B2 | 20010412 | | |
| EP 1010705 | A1 | 20000621 | EP 1998-940649 | 19980901 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| ZA 9808023 | A | 19990302 | ZA 1998-8023 | 19980902 |
| NO 2000001045 | A | 20000427 | NO 2000-1045 | 20000301 |
| PRIORITY APPLN. INFO.: | | | | |
| | | | JP 1997-237481 | A 19970902 |
| | | | JP 1998-63270 | A 19980313 |
| | | | WO 1998-JP3893 | W 19980901 |

OTHER SOURCE(S): MARPAT 130:237885

AB Claimed are cyclic tetrapeptide derivs. represented by general formula (I) or pharmaceutically acceptable salts thereof and cyclic tetrapeptide compds. analogous thereto [wherein R11, R12, R21 and R22 represent each hydrogen or a monovalent group selected from linear or branched C1-6 alkyl, benzyl, 4-methoxybenzyl, 3-indolylmethyl, (N-methoxy-3-indolyl)methyl, (N-formyl-3-indolyl)methyl, etc.; R3 represents a divalent group selected from divalent linear C3-4 hydrocarbyl optionally having a branched chain added thereto or optionally substituted by a heteroatom; and R4 represents a divalent group derived from divalent linear C4-6 hydrocarbyl optionally having a branched chain added thereto]. Also claimed are histone deacetylase inhibitors, MHC class-1 mol. expression promoters, and anticancer agents contg. these cyclic tetrapeptide derivs. as the active ingredient. The hydroxamic acid side chain is responsible for the activity of MHC class-1 mol. expression promotion. These cyclotetrapeptides markedly promote the removal of cancer cells by immune cells using promotion of MHC-1 mol. expression, since they also inhibit cell proliferation and cell cycles, thereby the expansion of cancer tissues, based on histone deacetylase inhibition. They are much more reduced in undesirable side-effects such as cell proliferation inhibition and cell cycle inhibition against normal cells as compared to irreversible enzyme inhibitors, since histone deacetylase enzyme inhibition is reversible. Thus, the title peptide (II) was prepd. via deprotection of Boc-Asu(OBzl)-D-Phe-Leu-DL-Pip-OtBu (Asu = .alpha.-aminosuberic acid residue, Pip = 2-carboxypiperidine residue) (prepn. given), cyclization, and conversion of the side-chain carboxylic acid into hydroxyaminocarbonyl group. II at 3.86 nM in vitro promoted twice the expression of MHC-1 mol. in mouse melanoma B16/BL6 cells as compared to 3.35 nM for trichostatin A and showed IC50 of 12.3 nM against the proliferation of B16/BL6 cells as compared to 14.3 nM for trichostatin A.

IC ICM C07K005-12

ICS A61K038-12

CC 34-3 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 1

| | | | | |
|-----------------|--------------|--------------|---------------------|--------------|
| IT 221186-39-6P | 221186-42-1P | 221186-43-2P | 221186-44-3P | 221186-45-4P |
| 221186-46-5P | 221186-47-6P | 221186-48-7P | 221186-49-8P | 221186-50-1P |
| 221186-51-2P | 221186-52-3P | 221186-53-4P | 221186-54-5P | 221186-55-6P |
| 221186-56-7P | 221186-57-8P | 221186-58-9P | 221186-59-0P | |
| 221186-60-3P | 221186-61-4P | 221186-62-5P | 221186-64-7P | 221186-65-8P |
| 221186-66-9P | 221186-67-0P | 221186-68-1P | 221186-69-2P | 221186-70-5P |
| 221186-71-6P | 221186-72-7P | 221186-73-8P | 221186-74-9P | 221186-75-0P |
| 221186-76-1P | 221186-77-2P | | | |

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of novel cyclic tetrapeptide derivs. as histone deacetylase inhibitors and MHC class-1 mol. expression promoters and anticancer agents)

IT 221186-59-0P

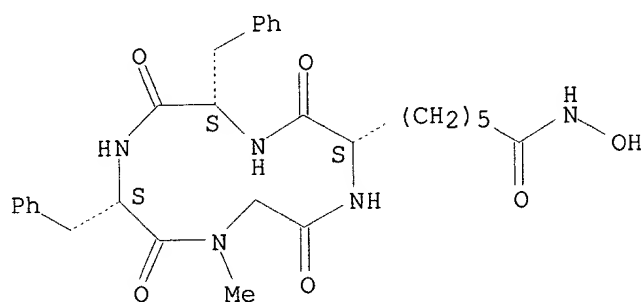
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of novel cyclic tetrapeptide derivs. as histone deacetylase inhibitors and MHC class-1 mol. expression promoters and anticancer agents)

RN 221186-59-0 HCAPLUS

CN Cyclo[N-methylglycyl-(2S)-2-amino-8-(hydroxyamino)-8-oxooctanoyl-L-phenylalanyl-L-phenylalanyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2

REFERENCE(S):

- (1) Bernardi, E; Peptides 1993, V14(6), P1091 HCAPLUS
- (2) Kijima, M; J Biol Chem 1993, V268(30), P22429 HCAPLUS

L8 ANSWER 7 OF 12 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1995:85675 HCAPLUS

DOCUMENT NUMBER: 122:131132

TITLE: Cyclic peptides manufacture with Flexibacter

INVENTOR(S): Teramura, Kyoko; Yasumuro, Kenichi; Suzuki, Yasuto; Shibazaki, Mitsuji; Abe, Kenji; Imai, Yoshimitsu; Suzuki, Kenichi

PATENT ASSIGNEE(S): Yamanouchi Pharma Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 14 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-------------|------|----------|-----------------|----------|
| JP 06172385 | A2 | 19940621 | JP 1992-351725 | 19921208 |

OTHER SOURCE(S): MARPAT 122:131132

AB Cyclic peptides (I, R1 = benzylcarbonyl, isovaleryl; R2 and R3 are OH individually or together as carbonyl) and II are manufd. by culturing Flexibacter sp. I and II are inhibitors for esterase of leukocytes and are useful for treatment of lung diseases such as ARDS.

IC ICM C07K005-12

ICS A61K037-02; C07K005-08; C12P021-02

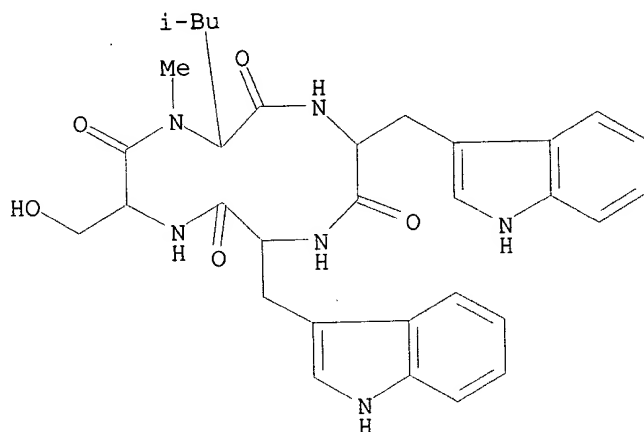
ICA C12N009-99

ICI C12P021-02, C12R001-01

CC 16-2 (Fermentation and Bioindustrial Chemistry)

IT 157951-38-7P 157951-39-8P, Cyclo(leucyltryptophyltryptophylseryl

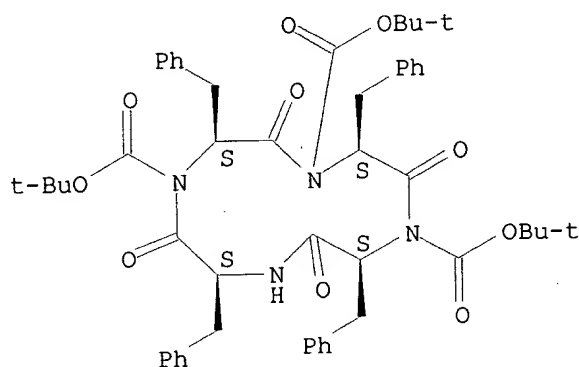
) 157951-40-1P
 RL: PREP (Preparation)
 (manuf of cyclic peptide, with Flexibacter for leukocyte esterase inhibitor)
 IT **157951-39-8P**, Cyclo(leucyltryptophyltryptophylseryl)
 RL: PREP (Preparation)
 (manuf of cyclic peptide, with Flexibacter for leukocyte esterase inhibitor)
 RN 157951-39-8 HCAPLUS
 CN Cyclo(leucyltryptophyltryptophylseryl) (9CI) (CA INDEX NAME)



L8 ANSWER 8 OF 12 HCAPLUS COPYRIGHT 2001 ACS
 ACCESSION NUMBER: 1994:164873 HCAPLUS
 DOCUMENT NUMBER: 120:164873
 TITLE: How to perform small peptide cyclizations
 AUTHOR(S): Cavelier-Frontin, Florine; Achmad, Sadijah; Verducci, Jean; Jacquier, Robert; Pepe, Gerard
 CORPORATE SOURCE: URA-CNRS 468 Aminoacides et peptides, Universite Montpellier II, Place Eugene Bataillon, Montpellier, 34095/05, Fr.
 SOURCE: THEOCHEM (1993), 105(1-3), 125-30
 CODEN: THEODJ; ISSN: 0166-1280
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Small cyclopeptides of four to six residues are very interesting for their biol. properties. Unfortunately, the synthesis of the linear precursor is generally fastidious and the cyclization often occurs in low yields. Mol. modeling used through the GENMOL program is a powerful tool for predicting the best precursor, as was shown in a previous paper about five tetrapeptides. However, sometimes all the linear precursors of a cyclopeptide can be unfavorable for cyclization when no structural feature (N-Me amino acid, Pro, D-amino acid) is present in the peptide. This led to the development of a method using a reversible chem. modification of the peptide main chain in order to favor the cisoid conformation able to cyclize easily. Tetra(phenylalanine) was used as a model, with the tert-butyloxycarbonyl (Boc) group as substituent on the main-chain nitrogen atoms. The cyclization yield increases from <1% to 27% after this chem. modification and cleavage of the Boc groups. Mol. modeling on such mols. shows that this yield increase is due to a preferred conformation having the terminal functions close together induced by the Boc substituents.
 CC 34-3 (Amino Acids, Peptides, and Proteins)
 Section cross-reference(s): 22

- IT 17528-16-4, L-Phenylalanine, N-[N-(N-L-phenylalanyl-L-phenylalanyl)-L-phenylalanyl]-methyl ester 153586-84-6 **153586-85-7**
 RL: RCT (Reactant)
 (cyclization of, effect of temporary protection on conformations for)
- IT **153586-85-7**
 RL: RCT (Reactant)
 (cyclization of, effect of temporary protection on conformations for)
- RN 153586-85-7 HCAPLUS
- CN Cyclo[L-phenylalanyl-N-[(1,1-dimethylethoxy)carbonyl]-L-phenylalanyl-N-[(1,1-dimethylethoxy)carbonyl]-L-phenylalanyl-N-[(1,1-dimethylethoxy)carbonyl]-L-phenylalanyl] (9CI) (CA INDEX NAME)

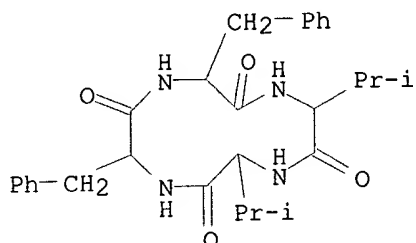
Absolute stereochemistry.



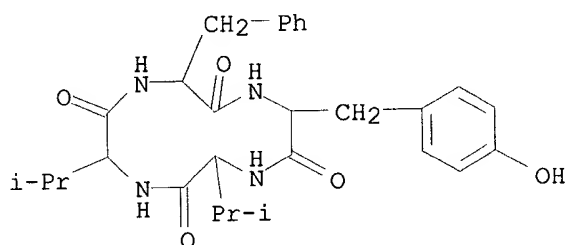
- L8 ANSWER 9 OF 12 HCAPLUS COPYRIGHT 2001 ACS
- ACCESSION NUMBER: 1980:406071 HCAPLUS
- DOCUMENT NUMBER: 93:6071
- TITLE: Gushing-inducing peptides in beer produced by *Penicillium chrysogenum*
- AUTHOR(S): Kitabatake, Katsuaki; Fukushima, Shuji; Kawasaki, Ichiro; Amaha, Mikio
- CORPORATE SOURCE: Cent. Res. Lab., Asahi Brew. Ltd., Tokyo, 143, Japan
- SOURCE: Pept. Chem. (1980), Volume Date 1979, 17th, 7-12
- CODEN: PECHDP
- DOCUMENT TYPE: Journal
- LANGUAGE: English
- AB A cyclic peptide that induced gushing in bottled beer was isolated from culture filtrates of *P. chrysogenum*. It was identified as cyclo-D-Val-L-Val-D-Phe-L-Phe (I) [**24181-12-2**]. Another factor inducing beer gushing was isolated that was a mixt. of I and other tetrapeptides contg. valine, phenylalanine, and tyrosine. The gushing caused by several natural and synthetic peptides was examd. and the results are tabulated. Cyclic structure was important; little or no gushing was induced by linear peptides.
- CC 16-3 (Fermentations)
- Section cross-reference(s): 34
- IT **24181-12-2**
 RL: BIOL (Biological study)
 (beer gushing caused by, from *Penicillium chrysogenum*)
- IT 2001-95-8 26048-05-5 38184-76-8 64763-82-2 68671-23-8 70274-72-5
 70274-74-7 70274-76-9 **73787-51-6** 73787-52-7 73787-53-8
 73787-54-9 **73804-19-0**
 RL: BIOL (Biological study)
 (beer gushing induction by)
- IT **24181-12-2**
 RL: BIOL (Biological study)
 (beer gushing caused by, from *Penicillium chrysogenum*)

Lukton 09/355,210

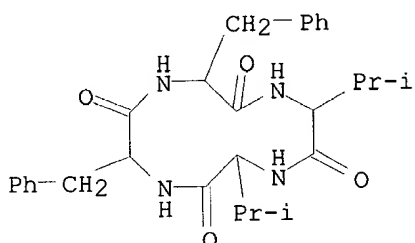
RN 24181-12-2 HCAPLUS
CN Cyclo(D-phenylalanyl-L-phenylalanyl-D-valyl-L-valyl) (9CI) (CA INDEX NAME)



IT 73787-51-6 73804-19-0
RL: BIOL (Biological study)
(beer gushing induction by)
RN 73787-51-6 HCAPLUS
CN Cyclo(D-phenylalanyl-L-tyrosyl-D-valyl-L-valyl) (9CI) (CA INDEX NAME)



RN 73804-19-0 HCAPLUS
CN Cyclo(L-phenylalanyl-D-phenylalanyl-L-valyl-D-valyl) (9CI) (CA INDEX NAME)



L8 ANSWER 10 OF 12 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1978:23373 HCAPLUS
DOCUMENT NUMBER: 88:23373
TITLE: Synthesis of biologically active cyclic peptides and
depsipeptides by the phosphite method
AUTHOR(S): Rothe, M.; Kreiss, W.
CORPORATE SOURCE: Org.-Chem. Inst., Univ. Mainz, Mainz, Ger.
SOURCE: Pept., Proc. Eur. Pept. Symp., 14th (1976), 71-8.
Editor(s): Loffet, Albert. Editions Univ. Bruxelles:
Brussels, Belg.
CODEN: 36PZAV
DOCUMENT TYPE: Conference

LANGUAGE:

English

AB H-(Val-D-Hyv-D-Val-L-Lac)n-OH [I; Hyv = OCH(CHMe₂)CO, Lac = OCHMeCO, n = 3] was cyclized by the phosphite method in toluene or diethyl phosphite (DEP) to give cyclo(Val-D-Hyv-D-Val-L-Lac)_m (II; m = 3) (valinomycin) in 24 or 56% yields, whereas I (n = 1, 2) were cyclized by the phosphite method in toluene or DEP to give II (m = 1-4, 6). II (m = 1) had a very stable crystal lattice and its IR spectrum gave no indication of cis peptide bonds. Antamanide (III) was prepd. by the phosphite-mediated cyclization of H-Phe-Phe-Val-Pro-Pro-Ala-Phe-Phe-Pro-Pro-OH (IV) or H-Pro-Ala-Phe-Phe-Pro-Phe-Phe-Val-Pro (V); IV always gave higher yields than V. Protected gramicidin S cyclo[Val-Orn(Pht)-Leu-D-Phe-Pro]_p (VI, Pht = phthalyl, p = 2), protected semigramacidin S VI (p = 1), and cyclo(D-Phe-Phe-D-Val-Val) (fungisporin) were also prepd. by the phosphite method.

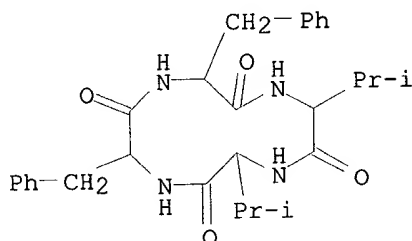
CC 34-3 (Synthesis of Amino Acids, Peptides, and Proteins)

IT 2001-95-8P 14410-23-2P 14735-43-4P 16898-32-1P 20696-06-4P
24181-12-2P 52611-33-3P 61491-09-6P 65034-96-0P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. of, by phosphite method)

IT **24181-12-2P**
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. of, by phosphite method)

RN 24181-12-2 HCAPLUS

CN Cyclo(D-phenylalanyl-L-phenylalanyl-D-valyl-L-valyl) (9CI) (CA INDEX NAME)



L8 ANSWER 11 OF 12 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1972:443496 HCAPLUS

DOCUMENT NUMBER: 77:43496

TITLE: Cyclic peptide analogs of gastrin

AUTHOR(S): Tritsch, G. L.; Sachatello, C. R.; Grahl-Nielsen, O.; Moriarty, C. L.; Sedwick, J.

CORPORATE SOURCE: Roswell Park Mem. Inst., New York State Dep. Health, Buffalo, N. Y., USA

SOURCE: J. Med. (Basel) (1971), 2(2), 82-5
 CODEN: JNMDBO

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Cyclic forms of 2 biol. active gastrin peptide analogs were synthesized and shown to be devoid of secretagogue activity on i.v. administration to dogs. In addn., the cyclic peptides were unable to inhibit the activity of an active secretagogue. The gastrin receptors seem to require not only the proper amino acid sequence but also a particular 3-dimensional conformation of biol. active analogs of gastrin.

CC 2-3 (Hormone Pharmacology)

IT **37792-55-5** 37792-56-6

RL: BAC (Biological activity or effector, except adverse); BIOL
 (Biological study)
 (biol. activity of)

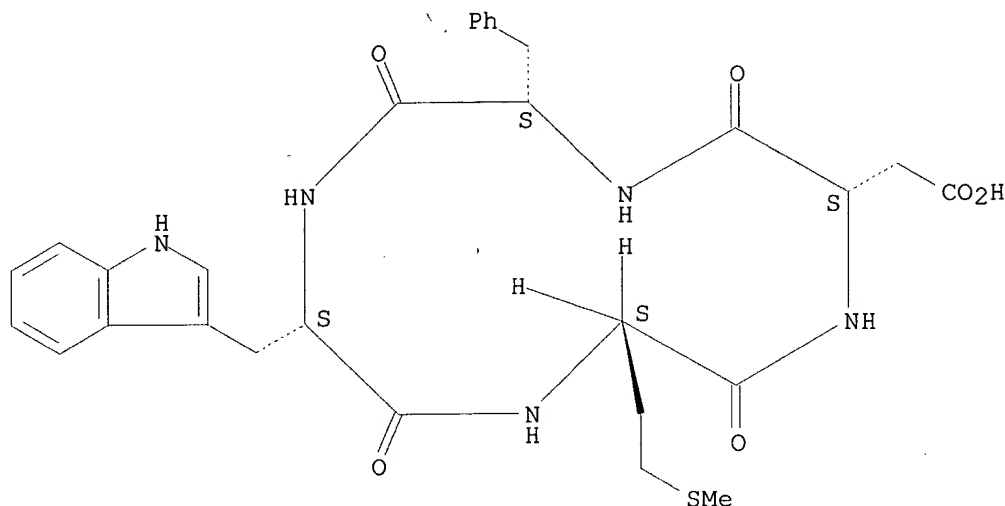
IT **37792-55-5**

RL: BAC (Biological activity or effector, except adverse); BIOL
(Biological study)
(biol. activity of)

RN 37792-55-5 HCAPLUS

CN Cyclo(L-.alpha.-aspartyl-L-phenylalanyl-L-tryptophyl-L-methionyl) (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 12 OF 12 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1969:524896 HCAPLUS

DOCUMENT NUMBER: 71:124896

TITLE: Synthesis and structure of fungisporin

AUTHOR(S): Studer, Rolf O.

CORPORATE SOURCE: Chem. Res. Dep., F. Hoffmann-La Roche and Co. A.-G.,
Basel, Switz.

SOURCE: Experientia (1969), 25(9), 899
CODEN: EXPEAM

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Fungisporin, a cyclooctapeptide, was previously reported as having the structure cyclo-(Phe-Val)₄. Sequence studies indicated cyclo-(D-Val-L-Val-D-Phe-L-Phe)₂. Z-L-Phe-D-Val-L-Val-D-Phe-O-Bu-tert (I) was prepd. by the stepwise elongation using the N-hydroxysuccinimide esters of the corresponding Z-amino acids. When I was treated with F₃CCO₂H, the tert-BuO group was removed and the resulting Z-tetrapeptide was activated with bis(p-nitrophenyl) sulfite and the Z group removed with HBr-AcOH. The p-nitrophenyl ester was cyclized under high diln. in pyridine to give a product with mol. wt. 482 by mass spectrometry which indicated a cyclic tetrapeptide. Natural fungisporin also has mol. wt. 482. (Z-PhCH₂O₂C)

CC 34 (Synthesis of Amino Acids, Peptides, and Proteins)

IT 24181-12-2

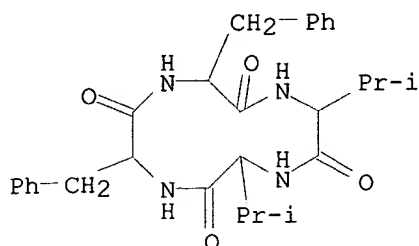
RL: PRP (Properties)
(structure of)

IT 24181-12-2

RL: PRP (Properties)
(structure of)

RN 24181-12-2 HCAPLUS

CN Cyclo(D-phenylalanyl-L-phenylalanyl-D-valyl-L-valyl) (9CI) (CA INDEX NAME)



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0 S L5

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CAS about this and ^{they} are
looking in to why there
is no reference to this
registry number. When I
get a reply from CAS I'll
let you know.

Alex

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